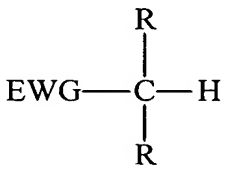
We claim:

1. A method for deprotection of an oligonucleotide comprising the step of reacting a protected oligonucleotide with a deprotection reagent wherein the deprotection reagent comprises an active methylene compound and an amine reagent,

wherein the active methylene compound has the structure:



where EWG is an electron-withdrawing group selected from nitro, ketone, ester, carboxylic acid, nitrile, sulfone, sulfonate, sulfoxide, phosphate, phosphonate, nitroxide, nitroso, trifluoromethyl and aryl groups substituted with one or more nitro, ketone, ester, carboxylic acid, nitrile, sulfone, sulfonate, sulfoxide, phosphate, phosphonate, nitroxide, nitroso, and trifluoromethyl; and

R is selected from hydrogen, C_1–C_{12} alkyl, C_6–C_{20} aryl, heterocycle and electron-withdrawing group;

whereby protecting groups are removed from the oligonucleotide.

2. The method of claim 1 wherein the protected oligonucleotide is covalently attached to a solid support through a linkage.

3. The method of claim 2 further comprising the step of cleaving the oligonucleotide from the solid support.

4. The method of claim 2 wherein the oligonucleotide remains covalently attached to the solid support after reacting with the deprotection reagent.

5. The method of claim 2 wherein the solid support comprises highly cross-linked polystyrene.

6. The method of claim 2 wherein the solid support comprises controlled-pore-glass.

7. The method of claim 2 wherein the solid support is a membrane which allows the deprotection reagent to pass through.

8. The method of claim 2 wherein the solid support is a frit which allows the deprotection reagent to pass through.

9. The method of claim 2 wherein the solid support is a planar, non-porous material.

10. The method of claim 9 wherein the material is glass, quartz, or diamond.

11. The method of claim 9 wherein the material is polystyrene, polyethylene, polypropylene, nylon, graft of polystyrene and polyethylene glycol, copolymer of ethylene and acrylate, or copolymer of ethylene and methacrylate.

12. The method of claim 2 wherein the solid support is positioned in a column having inlet and outlet openings whereby reagents may flow through the column.

13. The method of claim 12 further comprising placing a plurality of such columns in a holder and concurrently deprotecting a plurality of oligonucleotides.

14. The method of claim 13 wherein the holder is a microtiter plate having an array of such columns.

15. The method of claim 1 wherein the protected oligonucleotide comprises at least one 2-cyanoethyl phosphate internucleotide linkage.

16. The method of claim 1 wherein the protected oligonucleotide comprises a nucleic acid analog.

17. The method of claim 16 wherein the nucleic acid analog is LNA.

18. The method of claim 16 wherein the nucleic acid analog is PNA.

19. The method of claim 16 wherein the nucleic acid analog is 2'-O-methyl RNA.

20. The method of claim 1 wherein the protected oligonucleotide is covalently attached to a label.

21. The method of claim 20 wherein the label is selected from the group consisting of a fluorescent dye, a quencher, biotin, a mobility-modifier, a minor groove binder, and a linker selected from C_1–C_6 alkylamine and C_1–C_6 alkylthiol.

22. The method of claim 21 wherein the minor groove binder is CDPI-3.

23. The method of claim 21 wherein the fluorescent dye is a fluorescein, a rhodamine, or a cyanine dye.

24. The method of claim 20 wherein the label is attached to the 5'-terminus of the polynucleotide.

25. The method of claim 20 wherein the label is attached to the 3'-terminus of the polynucleotide.

26. The method of claim 1 wherein the deprotection reagent further comprises water.

27. The method of claim 1 wherein the deprotection reagent further comprises an alcohol solvent.

28. The method of claim 27 wherein the alcohol solvent is methanol.

29. The method of claim 27 wherein the alcohol solvent is ethanol.

30. The method of claim 27 wherein the alcohol solvent is ethylene glycol.

31. The method of claim 1 wherein the active methylene compound is 2,4-pentanedione.

32. The method of claim 1 wherein the active methylene compound is 1,3-cyclohexanedione.

33. The method of claim 1 wherein the active methylene compound is ethyl acetoacetate.

34. The method of claim 1 wherein the active methylene compound is malononitrile

35. The method of claim 1 wherein the active methylene compound is malonic acid.

36. The method of claim 1 wherein the active methylene compound is nitromethane.

37. The method of claim 1 wherein the active methylene compound is malonamide.

38. The method of claim 1 wherein the active methylene compound is a dialkylmalonate diester wherein the alkyl groups are C_1–C_6 alkyl.

39. The method of claim 1 wherein the deprotection reagent comprises a mixture of a dialkylmalonate diester wherein the alkyl groups are C_1–C_6 alkyl, aqueous ammonium hydroxide, and an alcohol solvent.

40. The method of claim 39 wherein the dialkylmalonate diester is dimethylmalonate.

41. The method of claim 39 wherein the dialkylmalonate diester is diethylmalonate.

42. The method of claim 39 wherein the dialkylmalonate diester is di-n-propylmalonate.

43. The method of claim 39 wherein the dialkylmalonate diester is diisopropylmalonate.

44. The method of claim 1 wherein the amine reagent is aqueous ammonium hydroxide.

45. The method of claim 1 wherein the amine reagent is aqueous methylamine.

46. The method of claim 1 wherein the amine reagent is ethylamine.

47. The method of claim 1 wherein the amine reagent is isopropylamine.

48. The method of claim 1 wherein the amine reagent is n-propylamine.

49. The method of claim 1 wherein the amine reagent is n-butylamine.

50. The method of claim 1 wherein the amine reagent is 1,2-ethylenediamine.

51. The method of claim 1 wherein the amine reagent is 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or 1,5-diazabicyclo[4.3.0]non-5-ene (DBN).

52. The method of claim 2 wherein said reacting step is effected by:

wetting the protected oligonucleotide covalently attached to the solid support with an active methylene compound and a solvent, and then

treating the protected oligonucleotide with an amine reagent.

53. The method of claim 52 wherein the solid support is confined in a column having inlet and outlet openings whereby reagents may flow through the column.

54. The method of claim 53 wherein a plurality of columns are configured in a holder whereby a plurality of oligonucleotides are deprotected concurrently.

55. The method of claim 55 wherein the holder is in a microtiter well configuration of equally spaced columns.

56. The method of claim 52 further comprising the step wherein the protected oligonucleotide and the amine reagent are placed in a sealable vessel whereby the oligonucleotide is deprotected.

57. The method of claim 52 wherein the amine reagent is aqueous ammonium hydroxide.

58. The method of claim 52 wherein the amine reagent is ammonia gas.

59. The method of claim 52 wherein the amine reagent is a C_1-C_6 alkylamine.

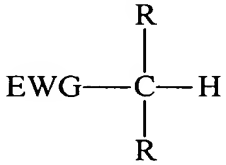
60. The method of claim 52 wherein the solvent is an alcohol, an ether, an amide, acetonitrile, dichloromethane, or dimethylsulfoxide.

61. The method of claim 60 wherein the alcohol is methanol, ethanol, n-propanol, isopropanol, or 1,2-ethylene glycol.

62. The method of claim 60 wherein the ether is diethyl ether, tetrahydrofuran, 1,4-dioxane, or 1,2-dimethoxyethane.

63. The method of claim 60 wherein the amide is acetamide, formamide, benzamide, or dimethylformamide.

64. An oligonucleotide deprotection reagent comprising an active methylene compound and an amine reagent wherein the active methylene compound has the structure



where EWG is an electron-withdrawing group selected from nitro, ketone, ester, carboxylic acid, nitrile, sulfone, sulfonate, sulfoxide, phosphate, phosphonate, nitroxide, nitroso, trifluoromethyl and aryl groups substituted with one or more nitro, ketone, ester, carboxylic acid, nitrile, sulfone, sulfonate, sulfoxide, phosphate, phosphonate, nitroxide, nitroso, and trifluoromethyl; and R is hydrogen, C_1–C_{12} alkyl, C_6–C_{20} aryl, heterocycle or electron-withdrawing group.

65. The oligonucleotide deprotection reagent of claim 64 wherein the active methylene compound is a dialkylmalonate diester and the amine reagent is aqueous ammonium hydroxide.

66. The oligonucleotide deprotection reagent of claim 65 wherein the dialkylmalonate diester is dimethylmalonate.

67. The oligonucleotide deprotection reagent of claim 65 wherein the dialkylmalonate diester is diethylmalonate.

68. The oligonucleotide deprotection reagent of claim 65 wherein the dialkylmalonate diester is di-n-propylmalonate.

69. The oligonucleotide deprotection reagent of claim 65 wherein the dialkylmalonate diester is diisopropylmalonate.

70. The oligonucleotide deprotection reagent of claim 65 wherein the active methylene compound is 1 to 10% by volume of the reagent.

71. The oligonucleotide deprotection reagent of claim 65 further comprising an alcohol solvent.

72. The oligonucleotide deprotection reagent of claim 71 wherein the alcohol solvent is 1 to 30% by volume of the reagent.

73. A deprotected oligonucleotide deprotected by the deprotection reagent of claim 64.

74. The deprotected oligonucleotide of claim 73 wherein the deprotected oligonucleotide comprises a nucleic acid analog.

75. The deprotected oligonucleotide of claim 74 wherein the nucleic acid analog is LNA.

76. The deprotected oligonucleotide of claim 74 wherein the nucleic acid analog is PNA.

77. The deprotected oligonucleotide of claim 74 wherein the nucleic acid analog is 2'-O-methyl RNA.

78. The deprotected oligonucleotide of claim 73 wherein the deprotected oligonucleotide is covalently attached to a label.

79. The deprotected oligonucleotide of claim 78 wherein the label is selected from a fluorescent dye, a quencher, biotin, a mobility-modifier, a minor groove binder, and a linker selected from C_1–C_6 alkylamine and C_1–C_6 alkylthiol.

80. The deprotected oligonucleotide of claim 79 wherein the minor groove binder is CDPI-3.

81. The deprotected oligonucleotide of claim 79 wherein the fluorescent dye is a fluorescein, a rhodamine, or a cyanine dye.

82. The deprotected oligonucleotide of claim 78 wherein the label is attached to the 5'-terminus of the polynucleotide.

83. The deprotected oligonucleotide of claim 78 wherein the label is attached to the 3'-terminus of the polynucleotide.